Final Assignment

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April 14, 2008

This document aims to present and criticize the article *"Algorithmic Self-Assembly of DNA: Theoretical Motivations and 2D Assembly Experiments"* written by Erik Winfree and appeared on the Journal of Biomolecular Structures and Dynamics in 2000.

First of all, let us consider the intended audience. As the name of the journal suggests, the article is addressed to biochemists and biotechnologists and not to theoretical computer scientists. Because of this, the outlay of the article and the elements that the author points out are quite different from the ones that a computer scientist is used to.

Content The title of the article is carefully chosen and it clearly summarizes the purpose of the whole article. In fact, Winfree presents the experimental "implementation" of a simple self-assembly process, i.e. he wants to demonstrate that double crossover molecules can be artificially designed such that they could simulate a Wang tiling process. The implications of this "controlled simulation" are remarkable in the context of the biomolecular computation by self-assembly molecules. The Wang's tiles are a computational model that was proved equivalent to the Turing Machine. Being able to reproduce and to control the dynamics of the Wang's computational model, even in simple cases as the one presented by the article, is the first essential step toward the effective realization of biomolecular computations.

The article mainly presents a review of the previous work of its author. As clearly stated at the end of the first section, Winfree summarizes the theoretical computational model, how it can be implemented by molecules, how the experimental simulation was done, and what results were obtained. In addition to a previous publication on Nature (1998), he gives an extensive characterization of the experiment and a deep analysis of the results.

Abstract The abstract starts by giving the context of the work that will be presented. In fact, it mentions the Adleman's experiment, that firstly showed the feasibility of a programmable biomolecular computation.

Then the author introduces the mechanism of DNA self-assembly by giving its theoretical foundations (the Wang's tiles) and asserting their equivalence (in term of computability expressiveness) to Turing Machines. He points out how the theoretical model can be biologically implemented by the Seeman's branched DNA constructions and why this is a wise choice.

He concludes illustrating the experiments that were done and the relevance of the work in a broader context.

Introduction and Examples The first part of the introduction is devoted to a retroperspective of the main results obtained by molecular computation, what future applications can be hypothesized, and what biological mechanisms to realize molecular computations were recently inspected by other researchers.

I think this part should end with a clear explanation of the structure of the rest of the article. Instead, it simply ends by saying that the article will present additional characterization of the experimental work previously published by the author. Probably the author omitted to clarify the structure of the article because a fixed structure of the article is required by the editors.

After this first part, the introduction contains two subsections: the first one introduces the tiling problem, while the latter one discusses how molecules can be designed in order to implement the theoretical model.

Computation by Tiling, i.e. the first subsection, contains a simple exposition of the tiling problem. The tone of the exposition seems adequate, considering that the intended audience is mainly composed by biologists and chemists. Moreover, several examples and figures help the readers understand what the tiling problem is and how computing by tiles is possible.

Four examples and four figures are presented. However an example uses a representation that is quite different from the other ones. I think that using heterogeneous pictorial representations is a bit confusing or, at least, unpleasant. Instead, the fifth example does not seem sufficiently described in the text. The main part of the description of the example is demanded to the caption of its figure.

Design of DNA crystal is the second subsection of the introduction. The author mixes two elements in this subsection: a general explanation of how Wang's tiles can be biologically realized, and what molecules were chosen for the subsequent experimentation. Actually, the figure that depicts the molecular structure of the tiles contains an error that is reported on the research group web page where the article can be downloaded.

I think that the article does not fit well in the fixed and rigid structure required by the editor. The introduction seems unnaturally long and it presents too much different elements to the readers. Moreover, the main results of the article, i.e. how well the self-assembly process was experimentally realized, were not clearly anticipated in the introductory part.

Main results The main results of the work relate to the feasibility of controlled and programmable simulation of Wang tiling by biochemical means. The third section of the paper extensively discusses the results obtained by the experimental work. Gel electrophoresis and

atomic force microscope imaging results are used to corroborate the author's claim. The analyses seem to be very accurate, and there are several well-commented figures.

However, there is no sentence saying that this technique can be applied to obtain more complex structures and/or computation. Instead, the interpretation of the results of the analyses are mainly left to an expert reader. Thus, it is quite difficult for a computer scientist to assess the quality of the results or the correct planning of the experiments and analyses.

This kind of articles requires a detailed description of the lab protocols, of the materials, and of the equipments that have been used. This description (section 2) should ensure the reproducibility of the experiments (and results) by independent research teams. This part is far less common in theoretical computer science publications.

Conclusions   The concluding part of the article summarizes the aim of the work that has been presented. Winfree emphasizes two conditions that any biomolecular realization of a self-assembly computation have to meet and he proposes a solution for each of them. He concludes discussing some more complex proposals for DNA computing that are recently aroused and that he finds particularly interesting and intriguing.

References   The bibliographic section contains 32 entries, that is not a small number considering the total length of the article. The cited works are quite recent (no more that 4 years before the publication) excluding the ones that refer to the tiling problem (that is an old problem studied in the '60 and the '70) and some very basic works (such as the Adleman experiment and the design of the DX molecules).

Technical delivery   I have some typographical remarks to point out. The style that has been chosen does not facilitate the navigability of the document. The titles of the sections and subsections are not sufficiently highlighted and some paragraphs are very close the captions of the figures, reducing the readability of the text. However, I downloaded the electronic copy from the research group's publications web page. Maybe it is the preprint of the article and these problems were addressed in the camera-ready version.